



END MASS OVERDOSE, INC.

Together We Can Be The Difference

OPIOID OVERDOSE EDUCATION & NARCAN TRAINING

Community Course 2017

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Objectives

- Define an opioid and explain the pharmacology of an opioid overdose
- List risk factors for opioid overdose
- Identify the signs of opioid overdose
- Evaluate how to respond to an opioid overdose using intranasal and intramuscular naloxone (Narcan)
- Analyze your role in the Opioid Epidemic

National Opioid Epidemic

259 million

- Number of prescriptions written for painkillers in 2012

Enough for *every American adult* to have one bottle of pills

20.5 million

- Number of people aged 12 years and older with a diagnosis of Substance Use Disorder in 2015

33,091

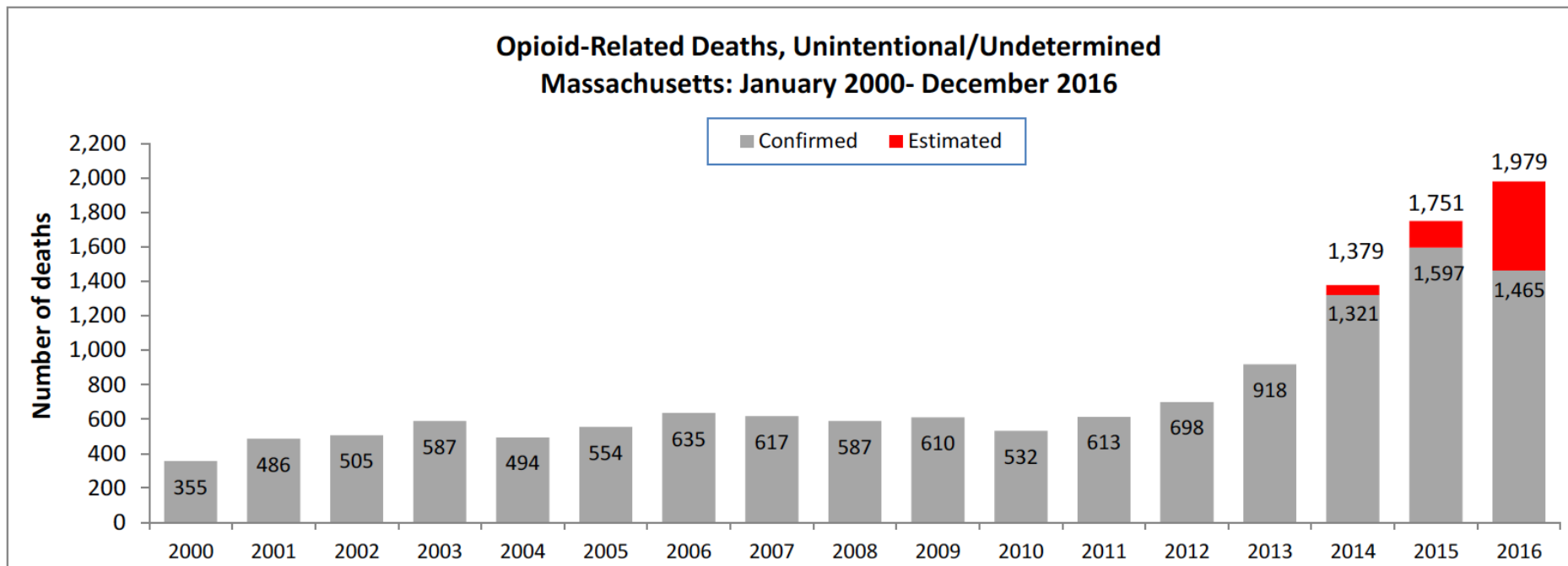
- Number of overdose deaths involving opioids in the United States in 2015
 - 20,101 related to prescription opioids, 12,990 related to heroin

1,979

- Estimated number of opioid overdose deaths in **Massachusetts** in 2015

5 more people will die in Massachusetts by the time we leave today

Opioid Epidemic Massachusetts



Over **550%** increase in opioid-related deaths
between 2000 - 2015

What is an opioid?

Is there a difference between an opiate and an opioid?

What is an Opioid?

Opiate versus Opioid

- **Opiate**: a natural substance derived from the opium poppy plant
- **Opioid**: a synthetic substance that acts on the opioid receptors to produce opiate-like effects

The term “opioids” refers to entire family, including natural opiates and their semi-synthetic and synthetic relatives

- Natural: morphine, codeine
- Semi-synthetic: heroin (diacetylmorphine)
- Synthetic: fentanyl, methadone, meperidine



Opioids

- Heroin
- Hydrocodone (Vicodin)
- Hydromorphone (Dilaudid)
- Morphine
- Methadone
- Oxycodone IR/ER (Percocet, Oxycontin)
- Oxymorphone (Opana)
- Fentanyl
- Buprenorphine (Suboxone, Subutex, Butrans)
- Codeine (Tylenol#3)
- Tramadol
- Diphenoxylate (Lomotil)

NOT Opioids

- Cocaine, Crack
- Methamphetamine
- Benzodiazepines (Valium, Klonopin, Xanax)
- Non-BZD hypnotics (Ambien)
- Alcohol
- Stimulants (Adderall, Ritalin)
- Marijuana
- MDMA (Molly, Ecstasy)
- Gabapentin (Neurontin)
- Sedatives (barbiturates)
- Psychedelics (LSD, peyote)

The Basics: Opioid Pharmacology

How do opioids work?

- Opioids are Central Nervous System (CNS) depressants
- Opioids attach to opioid receptors in the brain, spinal cord, gastrointestinal tract, and other organs

Major indications for Medical Use

- Pain relief- reduce perception of pain in the brain
- Cough- suppress cough reflex in the brain (codeine)
- Diarrhea- suppress gastrointestinal tract motility (diphenoxylate)

What is an opioid overdose?

What is an opioid overdose?

Opioid Overdose:

- Acute condition due to excessive exposure to opioids
- Dysfunction of the normal breathing mechanism

What is an opioid overdose?

Normal breathing mechanism

- Respiratory center detects and responds to low levels of oxygen and high levels of carbon dioxide in the blood
- Respiratory drive is functional

Opioid-present breathing mechanism

- Opioids attach to receptors in the brain responsible for breathing → suppress the respiratory center (no longer responds)
- Breathing slows → unresponsive → respiratory depression
- Brain damage occurs within **3-5 minutes without oxygen**

Intervention is key! Overdoses are rarely an instantaneous process

Where are the opioids coming from?

Where are the opioids coming from?

How many people addicted to heroin started on prescription painkillers?

75%

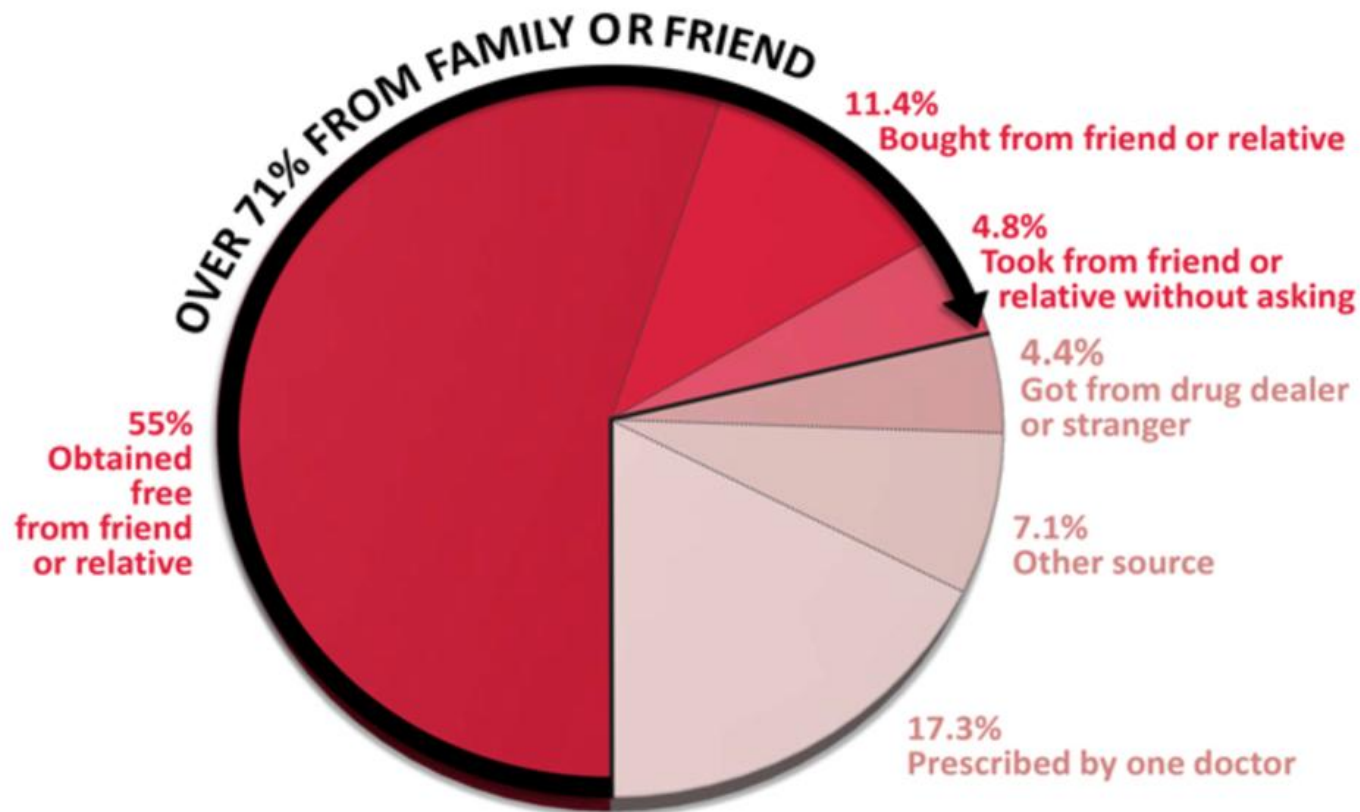
“When you look at the effects that opioids and heroin produce, it is indistinguishable.” -Dr. Andrew Kolodny

New laws and guidelines: **focus on treating underlying disease, not treating symptoms**

National Opioid Epidemiology

Where are people obtaining prescription opioids?

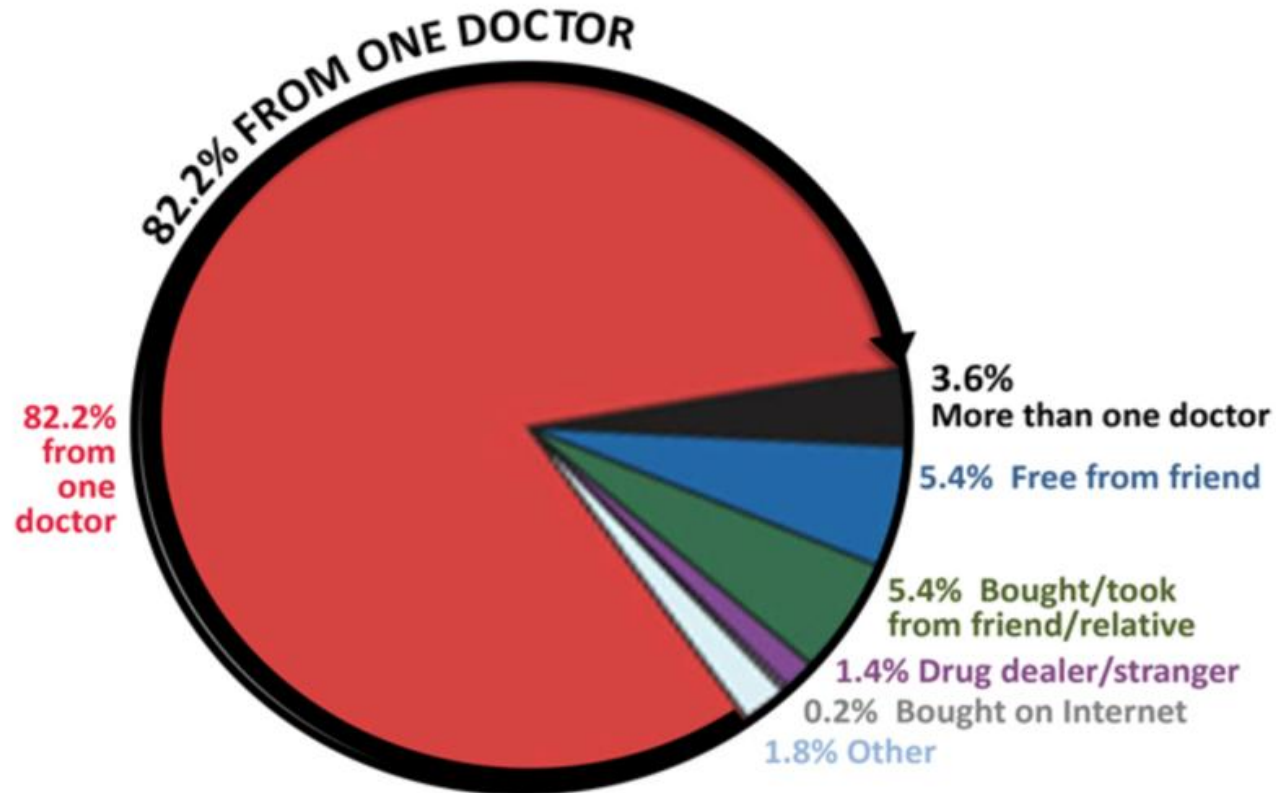
Where Prescription Opioids are Obtained



National Opioid Epidemiology

Where are our friends and family members getting prescription opioids?

Where Family and Friends Get Opioids



Who is at risk for an opioid overdose?

Risk Assessment

List risk factors for opioid overdose

- Tolerance
- Opioid prescriptions
- Polysubstance Use
- Chronic Medical Conditions
- Unsafe Social History

Risk Factor: Tolerance

- Tolerance develops with frequent, extended, or chronic use
 - Extended = 30 days Chronic = 90 days

↑ tolerance → ↑ drug quantity needed to achieve same effect/high

- Tolerance **rapidly reduces within a few days** of abstinence
 - Periods of abstinence include: hospitalization, incarceration, detox or drug treatment, stopping on one's own, opioid unavailability

Risk Factor: Opioid RXs

- Large quantity and/or high daily dose
 - Daily dose ≥ 50 mg morphine equivalents
- Receiving prescriptions for multiple opioids at one time
- Being prescribed an opioid + another CNS depressant
- Medication rotation in chronic pain management, incomplete cross tolerance



Risk Factor: Polysubstance Use

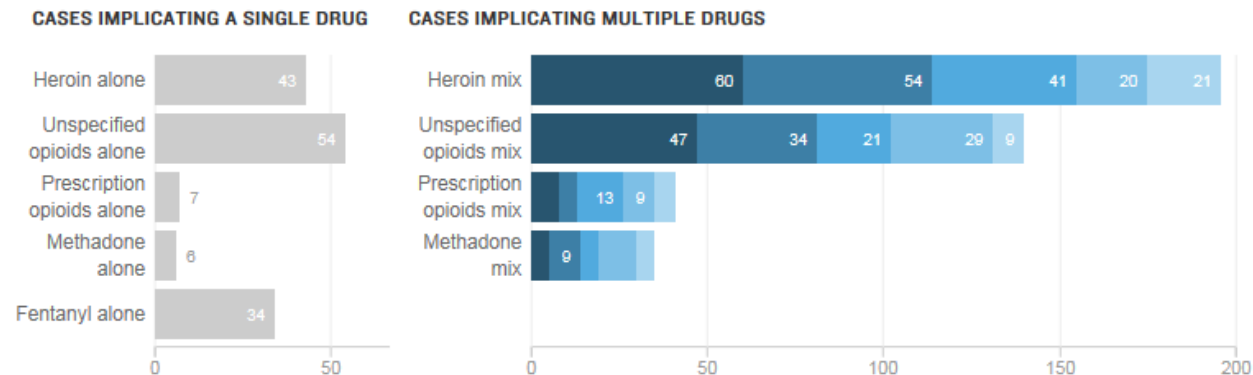
In addition to heroin, what are the most common drugs found in an opioid overdose in Massachusetts?

Most Overdose Deaths In Massachusetts Involve Multiple Drugs

Number of overdose deaths in Massachusetts, January through June 2014

Drugs combined with:

None Fentanyl Cocaine Alcohol Benzodiazepines Miscellaneous prescribed opioids



Notes

Drug combinations are classified in pairs of drugs only. Cases involving more than two drugs are counted in each category they fall under.

Source: [Vaughan W. Rees and Christopher D. Knapp, Harvard T.H. Chan School of Public Health](#)

Credit: Katie Park/NPR

501 overdose deaths assessed by the MA Office of the Chief Medical Examiner in first 6 months of 2014, **fentanyl** was present in **37%** and **benzodiazepines** present in **13%**

Risk Factor: Polysubstance Use

Benzodiazepines, Alcohol, CNS Depressants

- Clonidine (Catapres), gabapentin (Neurontin) = street value
 - Antihistamines: diphenhydramine (Benadryl), hydroxyzine (Vistaril), doxylamine (Unisom), cimetidine (Tagamet), promethazine (Phenergan)
 - Dextromethorphan (Robitussin)
-
- Overlapping side effects, intensify sedative effects of opioid
-
- When combined, have synergistic (additive) effect that increases risk of respiratory depression

Risk Factor: Polysubstance Use

Psychiatric Quarterly (2001) self-report survey

- 93% of opiate dependent respondents seeking treatment knew of clonidine abuse. Used to decrease amount of heroin needed to achieve desired high and to prolong the length of opiate's action

American Journal of Addiction (2015) self-report questionnaire

- 162 patients with opioid dependency: 28% of those with a prescription reported using higher amounts of each medication than prescribed.
- 10% reported misusing clonidine, 22% gabapentin, 7% pregabalin, 25% clonazepam, 11% amphetamine salts, 36% any of these medications

Dennison SJ. Clonidine abuse among opiate addicts. *Psychiatr Q.* 2001 Summer; 72(2):191-5.

Wilens T1, Zulauf C, Ryland D, Carrellas N, Catalina-Wellington I. Prescription medication misuse among opioid dependent patients seeking inpatient detoxification. *Am J Addict.* 2015 Mar;24(2):173-7. DOI: 10.1111/ajad.12159.

Risk Factor: Polysubstance Use

- Gabapentin abuse occurs internationally. Abuse may be specific to the opioid addicted population

Addiction Journal (2016)

- Systematic review of epidemiological and case reports from United States, United Kingdom, Germany, Finland, India, South Africa, France
- Prevalence of gabapentin misuse in general population was 1%, 40-65% in individuals with prescriptions ,15-22% in opioid abuse population

Risk Factor: Polysubstance Use

Psychiatric Quarterly (2016)

- Bastiaens et al. concluded gabapentin abuse is associated with opioid addiction
- 250 former inmates with dual diagnosis of substance use disorder + a psychiatric condition. Opioid use disorder (OUD: $n = 145$), 26 % endorsed illegally obtaining, overusing, abusing gabapentin. Only 4 % without an OUD ($n = 105$) endorsed non-medical use of gabapentin. (Chi square $\chi^2 = 21.6$, $p < 0.0001$)

Patriot Ledger (2015)

- July 2015 Norfolk County District Attorney Mike Morrissey and Senator John Keenan testify in favor of a bill to require gabapentin to be added to MA PMP
- In Quincy alone, 40% of 125 heroin overdoses last reported, 15 being fatal
- Gabapentin is widely used as a form of currency on the street for purchasing and bartering for opioids in MA

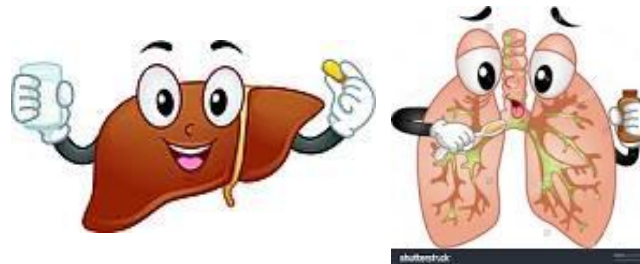
Risk Factor: Polysubstance Use

Stimulants

- Cocaine, methamphetamine, Adderall (amphetamine salts), methylphenidate (Ritalin/Concerta)
- Speed balling = mixing opioid + stimulant
 - Common misconception = stimulant counterbalances effects of opioid. Decreases risk of overdose while allowing the user to still get high
- Stimulant: causes vasoconstriction → reduces blood flow to the brain, increases heart rate, body uses more oxygen
- Opioid: slows breathing rate, less oxygen is entering
- **Dangerous Cycle/ Accumulation of Side Effects**: *Increased demand for oxygen (due to stimulant) is not met by decreased supply (due to opioid)*

Risk Factor: Chronic Health Conditions

- Kidney or liver dysfunction or disease
 - Cannot metabolize or clear drug, leading to buildup
- Respiratory conditions
 - Current smoker, asthma, COPD, emphysema, obstructive sleep apnea, respiratory infection or illness



Risk Factor: Unsafe Social History

Previous Nonfatal Overdose

- Previous overdose may have damaged the brain, lungs, vital organs
- Impaired functioning makes future overdoses more likely to be fatal

Chipping

- Chipping: using opioids or heroin intermittently or scheduled as an attempt to moderate use or to “prevent becoming an addict”
- Example: only on weekends, every 72 hours, every 8 hours, twice daily
- Does not decrease the likelihood of overdose

Using Alone**

- No one around to administer naloxone

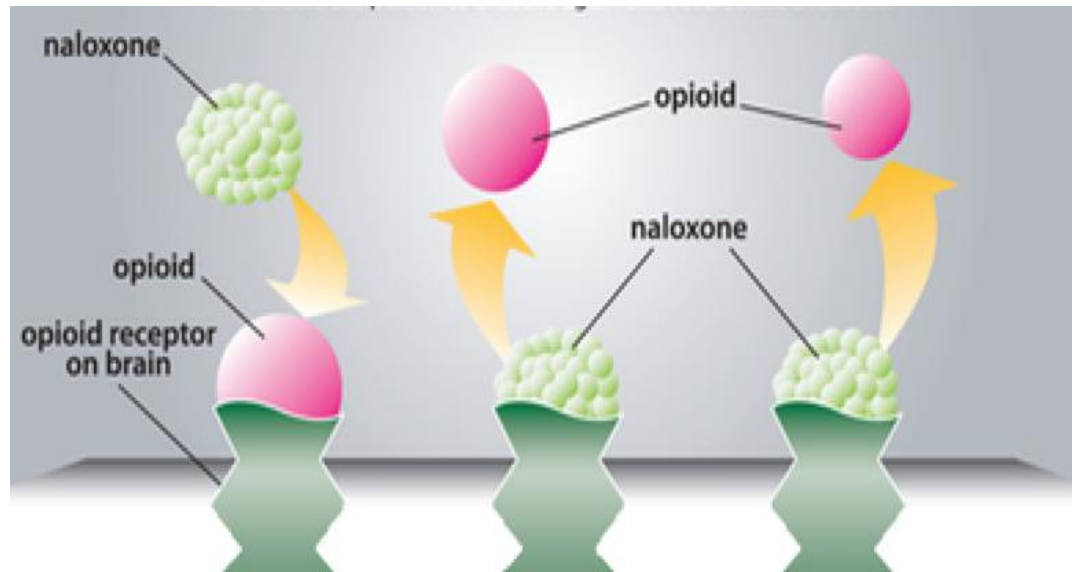
How to Respond to an Overdose

What is Narcan (Naloxone)?

- Medication that blocks and/or reverses the effects of opioids
- CVI **prescription** in Massachusetts

Mechanism of Action:

- Opioid antagonist with greatest affinity for the mu receptor
- Acts by competing for the mu, kappa, and sigma opiate receptor sites in the Central Nervous System (CNS)
- Binds to receptors → displaces opioid and reverses respiratory depression



Narcan (Naloxone) Pharmacokinetics

How long does it take naloxone to work?

- Onset of action: immediately or up to 8 minutes
 - Rule of thumb: re-administer if minimal or no response in 2 minutes
- Duration of action: the effects last 30 to 90 minutes
 - Rule of thumb: 60 minutes

Can naloxone be used to reverse all overdoses?

- **NO!** Only effective in overdoses involving **opioids**.
- No effect in the absence of opioids. Will not reverse an overdose from pure cocaine, benzodiazepines, alcohol, etc.

When & How to Administer Narcan

Opioid Overdose Response

1. Assess the situation. Call 911
2. Administer Narcan
3. Rescue breathing (if needed)
4. Victim observation
Ensure victim receives medical attention

Step 1: Assess the Situation

Intoxication “high” versus Overdose

HIGH	OVERDOSE
Relaxed muscles Normal skin tone	Limp body, pale, clammy skin Blue lips, fingertips
Slowed or slurred speech Normal breathing	Not speaking Infrequent or no breathing
Sleepy looking Drowsy, but arousable	Deep snoring, gurgling Not arousable
Responsive to stimuli including yelling, sternal rub	Not responsive to stimuli
Normal heartbeat	Slow or irregular heartbeat

Step 1: Assess the Situation

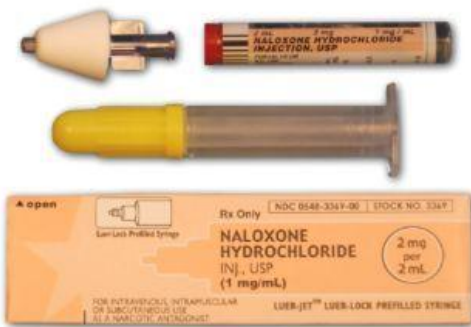
- Vomiting
- Passing out, heavy “nodding” off
- Awake, but unable to talk
- Choking, gurgling, snoring sounds, the “Death Rattle”
- **Breathing is slowed, irregular, or stopped completely**
- **Unresponsive**
- **Miosis (pinpoint pupils)**

Tip: if someone is making unfamiliar sounds while “sleeping,” try rousing the person. Many bystanders think a person is snoring when they are in fact overdosing

Step 1: Assess the Situation

1. Identify if the person is responsive, arousable, and breathing
2. Attempt to stimulate the person
 - Yell their name
 - Sternal rub
 - Make a fist, apply pressure by rubbing the knuckles up and down the sternum or breastbone (necktie area)
 - Under the nose rub
 - Make a fist, apply pressure by rubbing the knuckles across the skin under the nose and above the upper lip
 - Preferred method if chest is inaccessible or chest injury is suspected

Step 2: Administer Narcan



Multi-Step Nasal Spray

1. Remove two yellow caps
2. Remove one red/purple cap
3. Attach nasal atomizer (spray device)

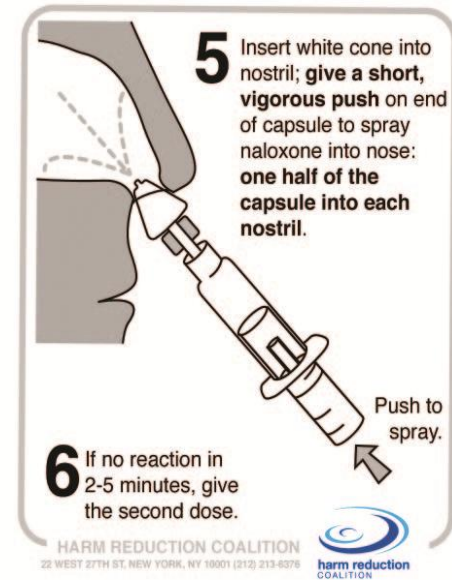
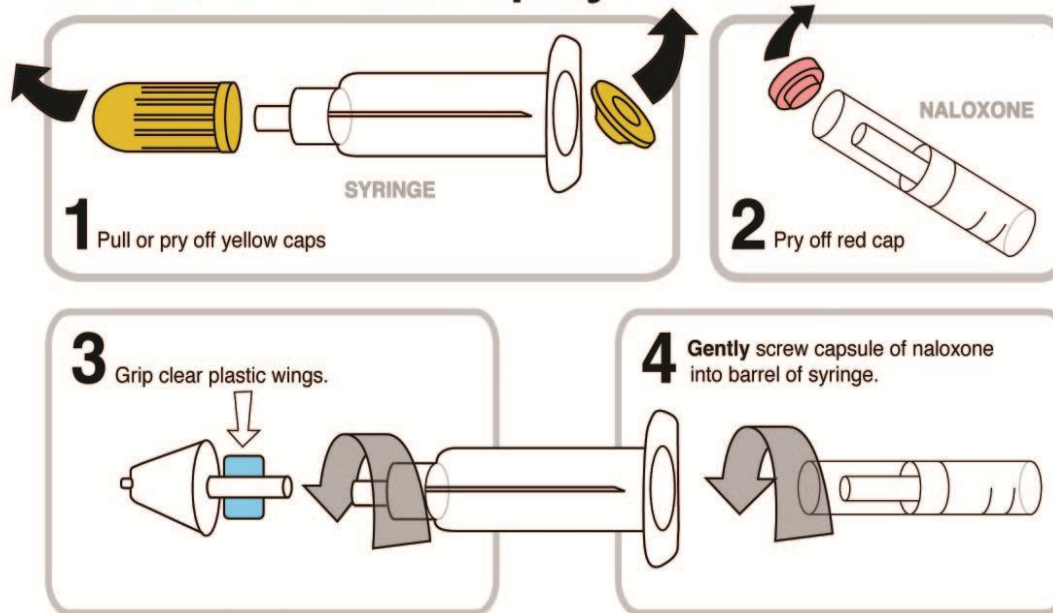


Screw atomizer onto the top of plastic delivery device

4. Insert and gently screw pre-filled medicine vial into the bottom of plastic delivery device
5. Spray half of the medicine (1 ml) in one nostril and spray the other half (1 ml) into the other nostril
6. If there is minimal or no response in 2 to 3 minutes, administer another dose
7. Rescue breathing if needed. Recovery position until help arrives

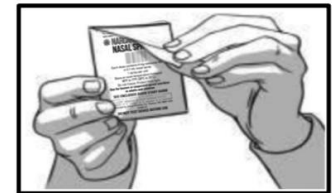
Multi-Step Nasal Spray

How to Give Nasal Spray Naloxone



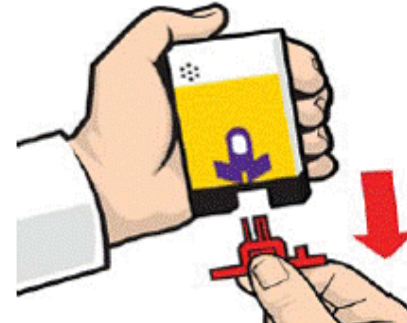
Single-Step Nasal Spray

1. Remove Narcan Nasal Spray from packaging
2. Place your thumb on the bottom of the plunger. Place your first and middle fingers on either side of the nozzle
3. Tilt person's head back and provide support under the neck with your hand
4. Insert tip of the nozzle into **one nostril** until your fingers are against the bottom of the person's nose
5. Firmly press plunger to deliver the **entire** dose
6. If minimal or no response in 2 to 3 minutes, administer second dose
7. Rescue breathing if needed. Recovery position until help arrives



Intramuscular Auto-Injector (Evzio)

1. Remove Evzio from outer case
 2. Pull off the red safety guard
 3. Place black end against middle of the outside thigh muscle, through the clothing
 4. Press firmly and hold in place for **5 seconds**
 5. If minimal or no response in 2 to 3 minutes, administer second dose
 6. Rescue breathing if needed. Recovery position until help arrives
- Voice instructions guide the way
 - Infants < 1 year old, pinch middle of thigh before administration



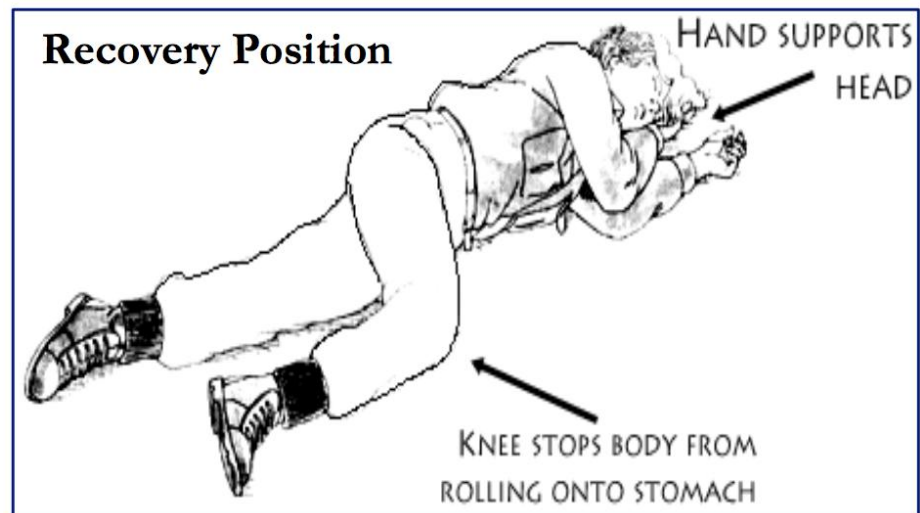
Step 3: Rescue Breathing

1. Place the person on their back
2. Check to see if there is anything in the person's mouth
3. Tilt their head back, lift chin, pinch nose shut
4. Give 2 breaths
 - Blow enough air into the lungs for chest to rise
5. Give one slow breath every 5 to 6 seconds until person starts breathing or help arrives



Step 4: Victim Observation

- Place victim in the recovery position
 - Lay person on his/her side, body supported by bent knee, with face turned to side
- Why observe? Why place in recovery position?
 - Half-life of opioid may outlast effects of naloxone. Victim should receive medical attention
 - Prevent aspiration







Opioid Overdose Response Review

SCARE ME

- **S**timulate
- **C**all 911
- **A**dminister naloxone
- **R**escue Breathing (if needed)
- **E**valuate. Give 2nd dose if needed
- **M**ove person to recovery position
- **E**valuate again. Stay until help arrives

Naloxone Quick Guide

	Naloxone Intranasal (Narcan)	Narcan Nasal Spray	Evzio	Naloxone Vial
				
Dose	2mg	4mg	0.4mg	0.4mg
Solution	2mg/2mL	4mg/0.1mL	0.4mg/0.4mL	0.4mg/1 mL
Route	Intranasal	Intranasal	IM auto injector	IM injection
Directions	Administer into both nostrils	Administer into one nostril	Inject into the anterolateral thigh	Inject into the anterolateral thigh or upper deltoid muscle
Onset of Action	2-8 min	2-8 min	2-5 min	2-5 min
Frequency	May repeat every 2-3min	May repeat every 2-3min	May repeat every 2-3min	May repeat every 2-3min
Features	Requires assembly	Ready to use, needle free	Voice instructions, ready to use	Multiple doses per vial, inexpensive

What should I NOT do in an overdose?

Do NOT:

- Put the person in a bath
- Induce vomiting
- Make the person drink something
- Put ice down the pants/crouch area or give a cold shower
 - Cooling down the core body temperature slows the heart rate and breathing rate, which increases the risk of shock and heart arrhythmia
- Try to stimulate person in a harmful manner
 - Punching, kicking, burning bottoms of feet
 - Person may respond to painful stimuli but it will not reverse the overdose
- Inject the person with anything (saltwater, milk)
 - Every injection increases the risk of a bacterial or viral infections

Clinical Considerations: Special Populations

Can I use Narcan on everyone?

Pregnancy

- Category C
- Crosses the placenta, may precipitate withdrawal in the fetus and the mother

Geriatrics

- Systemic exposure may be higher- greater frequency of decreased hepatic, renal, cardiac function

Nursing Mothers

- Unknown if excreted into breast milk

Pediatrics

- Safety and effectiveness established with well-controlled studies

Troubleshooting with Narcan (Naloxone)

Lost or Broken Atomizer

Broken Narcan (Naloxone) Vial

Unable to Atomize Solution

- Call 911 and administer by squirting or pouring the naloxone (Narcan) solution directly into the nostril
- Perform rescue breathing until help arrives.
- Do not pour naloxone solution into the victim's mouth

Bioavailability!

Intranasal administration = direct absorption into the blood stream through the nasal cavity, avoids gastrointestinal destruction and hepatic first pass metabolism

Troubleshooting with Narcan (Naloxone)

Nose Bleed

Expired Narcan

- Call 911 and administer regardless
- Perform rescue breathing until help arrives
- Substantial nasal bleeding may interfere with absorption
- Narcan's full efficacy is not guaranteed beyond the expiration date but it will **not hurt** the person and may provide some benefit

Incorrect Administration

- If you administered the full dose of multi-step intranasal Narcan into one nostril, Do not panic.
- Wait 2 minutes, if minimal or no response, administer a 2nd dose correctly. One-half in each nostril.

Commonly Asked Questions

Can Narcan reverse an overdose involving buprenorphine products (Suboxone, Zubsolv)?

- Yes, but not as well. Risk of limited efficacy.
- Larger or repeat doses may be required due to buprenorphine's long duration of action and slow rate of dissociation from opioid receptors

Can I keep Narcan in my car? Where can it be stored?

- Store at room temperature in cool, dark place. Protect from light

Can I pre-assemble multi-step intranasal Narcan?

- The shelf life of assembled prefilled syringe is only 2 weeks.
- Recommendation: Do not insert naloxone (Narcan) vial until ready to administer

Commonly Asked Questions

Can Narcan get you high?

- **No.** It has no potential for abuse or dependency. It has no effect in the absence of opioids

Can Narcan hurt someone?

- Serious side effects are rare
- Common side effects are opioid withdrawal symptoms
 - Irritability, anxiety, nervousness, aches, muscle spasms, upper body secretions (sweating, runny nose, tears), flushing, diarrhea, nausea, vomiting, tachycardia
- Risk of withdrawal symptoms increases with larger doses and extent of a person's drug dependency (opioid-dependent)
- To prevent opioid withdrawal symptoms, small doses are titrated and given over time until desired effect is achieved in a controlled medical setting

Commonly Asked Questions

Can Narcan cause an overdose?

- **No.** Larger doses may cause symptoms of opioid withdrawal

Can I develop a tolerance to Narcan? Will Narcan work on someone who has previously used it?

- **No** cannot develop tolerance to naloxone
- Can be used in every opioid overdose situation regardless of previous uses
- People may respond to naloxone differently each time, but this is likely due to the type or combo of drugs ingested, how old the naloxone is, how it has been stored.

Commonly Asked Questions

What if it wears off or doesn't work? Can I give multiple doses of Narcan?

- **Yes.** Long acting opioids last longer than 30-90 minutes. Thus, several doses may be required

After an overdose is reversed, should the victim go to the hospital?

- **Yes.** Victim should be observed for up to 6 hours to ensure s/he does not go back into an overdose when naloxone wears off
- If victim refuses to go to hospital, bystander should observe him/her

What if the victim is wearing a fentanyl patch?

- Remove patch with covered hands. Use gloves or sleeves to prevent absorption. After patch removal, call 911 and administer Narcan.

Common Legal Questions

- Prescriber immunity from criminal prosecution for prescribing, dispensing or distributing naloxone to a layperson: **YES**. MGL c. 94C § 19
- Layperson immunity from criminal liability when administering naloxone? **YES**. MGL c.94C § 34A
- Can I carry naloxone? Law removes criminal liability for possession of naloxone (possession w/out a RX)? **YES**. MGL c.94C § 34A
- Third party prescribing allowed: **YES**

Common Legal Questions

- Good Samaritan Law: **YES**. 94C, § 34A

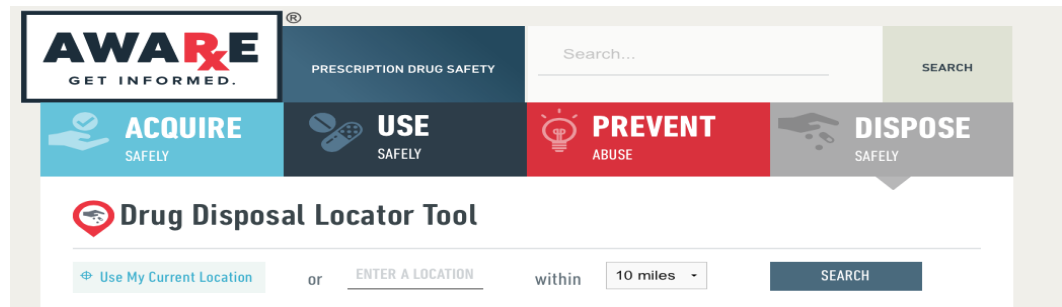
Immunity from being charged or prosecuted for possession of a controlled substance if evidence for the charge was gained as a result of the seeking of medical assistance during an overdose

- *Goal: to reduce the fear of calling 911*
- Does not protect a person from being charged with trafficking, distribution, or possession with intent to distribute

Most fatal overdoses are polysubstance. Due to this complexity, an overdose is a medical emergency. Call 911

The Role of Community Members

- Narcan (Naloxone) Education
 - Provide information about naloxone, its use, ability to obtain with or without a RX, where to obtain it
- Combat Stigma
 - Community Awareness Events
- Dispose of unused medications
 - Bring to local police station, town hall, or other medication disposal site
 - Use the National Association of Boards of Pharmacy (NABP) AwareRx Drug Disposal Locator tool: <http://www.awarerx.pharmacy/dispose-safely/disposal-sites>



The Role of Family and Friends

- Vigilance
 - Monitor risky behavior or changes in behavior, identify red flags, and respond. Early intervention is key.
- Root cause analysis of substance abuse
 - Identify motivating reasons/factors for misuse to treat underlying issues
 - Relapse is often related to unaddressed underlying factors
 - Treat therapeutically. Encourage clinicians to place misuse behaviors on the *patient's problem list* to address therapeutically.
 - Evaluate if proper medical and psychosocial support systems are in place

Where Can I Get Naloxone (Narcan)?

- CVS #394: 1479 Newman Ave, Seekonk MA
- CVS #16719: 79 Commerce Way, Seekonk MA
- Anawan Pharmacy: 224 Winthrop St, Rehoboth MA
- CVS #1864: 191 North Main St, Attleboro MA
- CVS #1896: 486 Pleasant St, Attleboro
- Walgreens #3020: 196 Pleasant St, Attleboro
- County Square Pharmacy: 289 County St, Attleboro MA
- CVS #6466: 2340 G.A.R. Hwy, Swansea MA

Question & Answers



References

- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition, Text Revision). Washington, DC: American Psychiatric Association; 2000:199-273.
- Center for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System, Mortality File. (2015). Number and Age-Adjusted Rates of Drug-poisoning Deaths Involving Opioid Analgesics and Heroin: United States, 2000–2014. Atlanta, GA: Center for Disease Control and Prevention. Available at [http://www.cdc.gov/nchs/data/health_policy/AADR_drug_poisoning_involving_OA_Heroin_US_2000 - 2014.pdf](http://www.cdc.gov/nchs/data/health_policy/AADR_drug_poisoning_involving_OA_Heroin_US_2000-2014.pdf).
- Centers for Disease Control and Prevention. (2014). Opioid Painkiller Prescribing, Where You Live Makes a Difference. Atlanta, GA: Centers for Disease Control and Prevention. Available at <http://www.cdc.gov/vitalsigns/opioid-prescribing/>.
- Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death 1999-2015 on CDC WONDER Online Database, released December, 2016. Data are from the Multiple Cause of Death Files, 1999-2015, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at [http://wonder.cdc.gov/ucd- icd10.html](http://wonder.cdc.gov/ucd-icd10.html)
- Centers for Disease Control and Prevention. Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics; 2016. Available at <http://wonder.cdc.gov>.
- Chang H, Daubresse M, Kruszewski S, et al. Prevalence and treatment of pain in emergency departments in the United States, 2000 – 2010. *Amer J of Emergency Med* 2014; 32(5): 421-31.
- Daubresse M, Chang H, Yu Y, Viswanathan S, et al. Ambulatory diagnosis and treatment of nonmalignant pain in the United States, 2000 – 2010. *Medical Care* 2013; 51(10): 870-878.

References

- Doering PL. Substance-related disorders: overview and depressants, stimulants, and hallucinogens. In: DiPiro JT, Talbert RL, Yee GC, et al, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 8th ed. New York, NY: McGraw-Hill Medical; 2011:1118.
- Green, TC, Dauria, EF, Bratberg, J, Davis, CS, Walley, AY. Orientation patients to greater opioid safety: models of community pharmacy-based naloxone. *Harm Reduction Journal*. 2015 Aug 6; doi: 10.1186/s12954-015-0058-x
- McCance-Katz E, Sullivan L, Nallani S. Drug interactions of clinically important along the opioids, buprenorphine and other frequently prescribed medications: a review. *Am J Addict*. 2010 Jan-Feb; 19(1): 4–16. doi: 10.1111/j.1521-0391.2009.00005.x
- National Institute on Drug Abuse. *Prescription Drugs: Abuse and Addiction*. NIH Pub No 11-4881. Revised October 2011. Available at: www.drugabuse.gov/sites/default/files/rprescription.pdf.
- National Institute on Drug Abuse. *Prescription Drug Abuse*. NIH Research Report. Revised November 2014. Available at: <https://www.drugabuse.gov/publications/research-reports/prescription-drugs/opioids/how-do-opioids-affect-brain-body>
- Rausch, T, Hellwig, T, Jones, B. Opioid education: key points for the pharmacist. *US Pharm*. 2012;37(5):31-35.
- Trescot AM, Boswell MV, Atluri SL, et al. Opioid guidelines in the management of chronic non-cancer pain. *Pain Physician*. 2006;9:1-39.
- Wheeler, E., Davidson, PJ, Jones, TS, Irwin, KS. Community-based opioid overdose prevention programs providing naloxone- United States, 2010. *MMWR Morb Mortal Wkly Rep*. 2012 Feb 17; 61(6): 101-105.